REMARKS

The Applicants acknowledge with thanks the withdrawal of rejections as noted in the most recent office action. The following remarks are believed to place the application in condition for allowance.

I. Non-Statutory Subject Matter

The Patent Office rejected claims 5-8 and 10 under 35 U.S.C. 101 for allegedly claiming non-statutory subject matter. (Office action pat paragraph 6.) Claim 5 has been amended to recite the term "isolated," rendering this allegation moot with respect to claim 5 and dependent claims 6-8 and 10. The Applicants continue to dispute the Patent Office's unsupported allegation that a transgenic host cell in a gene therapy context is nonstatutory subject matter.

II. Lack of Specific and Substantial Utility

The Patent Office rejected claims 1, 4-8, 10, 51-55, and 70 under 35 U.S.C. 101 for allegedly lacking specific and substantial utility. (Office action at paragraph 7.)

A. Utility as a marker for the testis

A first specific, substantial, and credible utility for polynucleotides of the invention is detection of testicular cells, because the gene corresponding to SEQ ID NO: 1 has been shown to be expressed predominantly in this cell type. The detection can be by way of using polynucleotides of the invention as probes to detect mRNA in a biological sample. Additionally, polynucleotides, vectors, and host cells of the invention can be used to express the protein encoded by SEQ ID NO: 1. Antibodies can be raised against the recombinant protein, and the antibodies can be used in standard immunoassays to detect the encoded protein expressed in cell membranes on the surface of cells.

As to this utility, the Patent Office alleged that "Applicants have failed to demonstrate the differential expression of the claimed polynucleotide as being expressed only in testicular cells and not in any other tissues" because "the instant polynucleotide was also detected in human testes, pancreas, a colon adenocarcinoma cell line and an ovarian carcinoma cell line." This low level expression in other tissues and cancer cell lines does not prevent use of polynucleotides of the invention to detect testicular tissue. There are few absolutes in the biomedical field, and absolute tissue specificity of gene expression is no exception. Scientists must generally be content with markers that are *predominantly* expressed in a single cell or tissue type, as is the case here. If a marker is shown to be predominantly expressed in only one tissue, then detection of a high level of expression in a biological sample normally indicates that a the sample contains that tissue. Moreover, when working with a marker that is predominantly expressed in a single cell type, a scientist with ordinary skill in the art is capable of adjusting the sensitivity of an assay so that low level expression (in other cell types) goes undetected. In this way, a marker that is "predominantly" express in one tissue behaves as a specific marker for that tissue under the particular assay conditions. In this regard, it is worth noting that the authors of Hulett et al. (of record) considered the expression of the gene corresponding to SEQ ID NO: 1 to be "testis specific."

The Patent Office further alleged that use "as a tissue specific marker is not a substantial or specific utility since testicular specific proteins were already known in the art." At the outset, the Patent Office has failed to substantiate this allegation. Morover, it is an irrelevant allegation. Because most tissue markers are not expressed absolutely exclusively by a single type of cell or tissue under all growth conditions, it is desirable to have two or more markers that are predominantly expressed on a single tissue or cell type of interest. The availability of multiple markers for a particular tissue permits identification of the tissue with a greater degree of confidence, and permits a practitioner to eliminate "false positives" from his detection assay. Thus, there is a continuing need for new markers that are predominantly expressed in a single cell or tissue type.

Moreover, the Patent Office has failed to cite any authority for the proposition that an invention must be the first or only invention to have a specific utility in order for the invention to be patentable. Neither the statute nor the Patent Office's reviewing court have ever imposed a "novel utility" requirement. The fact that other polynucleotides or proteins

might have the same specific utility -- that of serving as a marker for testicular cells -- does not negate the fact that the polynucleotide of the invention has this specific utility.

The Patent Office further alleges that "all human proteins can invariably be classified into two categories, those which are expressed in a tissue or developmentally specific manner and those which are expressed ubiquitously. Even if true, the Patent Office's allegations about all human proteins is irrelevant to the statutory inquiry. The MPEP provides guidance that use as a probe "would not be considered to be *specific* in the absence of a specific target." In the present case, the applicants teach that the testes are a specific target, and no more can be required.

The Patent Office tries to draw an analogy to use as a molecular weight marker. The analogy is misplaced. A molecular weight marker is useful as such by virtue of size, a fungible property. The polynucleotide of the invention is useful as a testis marker by virtue of its unique sequence and the expression pattern of a corresponding unique gene in the testis.

B. Utility as a chromosomal marker

Another utility -- also discussed in the Applicants' prior amendment -- is as a chromosomal marker for chromosome 11 (11q12-13), a region to which chromosomal aberrations have been linked to pathologies. It is well known that chromosomal markers are useful for screening for the presence of, and characterizing the nature of, chromosomal aberrations.

Again, the Patent Office's principal objection to this utility is an objection based upon the poor analogy to a molecular weight marker. The analogy is misplaced. A chromosomal mapping location is like real estate -- every location is unique. While using a protein as a molecular weight marker or as an analytical standard constitutes a general use that can apply to virtually any protein, the polynucleotide SEQ ID NO: 1 is specifically located in a particular region on a particular human chromosome. There is only one gene at the exact locus on chromosome 11 corresponding to SEQ ID NO: 1, and a limited number of nearby

neighbors that can be said to map to 11 q12-13. The fact that other pieces of DNA may map to other locii on human chromosomes is irrelevant.[1]

The Patent Office also alleged that the asserted utility is inadequate because "Applicants have not presented evidence that the instant nucleic acid has anything to do with non-Hodgkin's lymphoma or any allergic diseases or any other disease or condition or that an alteration in this gene has anything to do with any disease or condition." However, the law does not require the Applicants to prove this nexus. The applicants have shown that the polynucleotide is useful as a marker for chromosome 11 (q12-13), and shown that rearrangements in this region are associated with the aforementioned conditions. The polynucleotides of the invention are useful in chromosomal analysis to screen for and identify such chromosomal aberrations. The ability to detect the aberrations in this region is sufficient to help with the diagnosis of these diseases/conditions and help elucidate the chromosomal aberration problem.

As a final argument, the Patent Office alleged that "To grant Applicant a patent on the claimed polynucleotide based solely upon an assertion that the polynucleotide can be employed as a chromosomal marker is clearly prohibited by this judicial precedent," citing *Brenner v. Manson*. However, the case being cited does not pertain to chromosomal markers or even to polynucleotides, and in fact, being over thirty-five years old, predates the entire biotechnology revolution. If the Patent Office is aware of any judicial precedent pertaining to utility as a chromosomal marker for a locus associated with aberrations and disease, the Applicants request that it be cited in the next Office action.

III. Lack of Enablement

The Patent Office maintained a rejection for lack of enablement on the same bases that it alleges lack of utility. For the reasons set forth in the preceding section, the application teaches a person of ordinary skill how to use the present invention, and the rejection should be withdrawn.

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[1] The Patent Office goes so far as to say that any nucleic acid can be used in genetic linkage analysis. This is an overstatement, because there is no basis for believing that a random nucleic acid will have any linkage to a human chromosome.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

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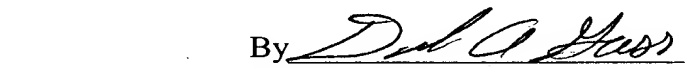
Respectfully submitted,

By 

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